

Applicant : Michael J. Detmar et al.
Serial No. : 09/536,087
Filed : March 24, 2000
Page : 3 of 22

Attorney's Docket No.: 10287-051001 / MGH 1470.0

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

D2
1. (Currently amended) A method of treating a subject having a disorder characterized by unwanted cell proliferation ~~an angiogenesis-dependent tumor~~, the method comprising administering to the subject a TSP-2 comprising an amino acid sequence at least 90% identical to the sequence of SEQ ID NO:2, or a fragment thereof capable of inhibiting endothelial cell migration, wherein the fragment comprises at least 10 contiguous amino acids of either (a) a procollagen domain of TSP-2, or (b) a type I repeat of TSP-2.

P7

2.-5. (Canceled)

6. (Previously presented) The method of claim 1, wherein the fragment comprises the sequence of SEQ ID NO:10 (WSPWAEW).

7.-13. (Canceled)

14. (Currently amended) The method of claim 13, wherein the disorder affects tumor is an epithelial tissue tumor.

15. (Currently amended) The method of claim 1, wherein the disorder tumor is characterized by unwanted a skin tumor cell proliferation.

Applicant : Michael J. Detmar et al.
Serial No. : 09/536,087
Filed : March 24, 2000
Page : 4 of 22

Attorney's Docket No.: 10287-051001 / MGH 1470.0

16. (Currently amended) The method of claim 15, wherein the ~~disorder~~ tumor is a squamous cell carcinoma of the skin or a malignant melanoma.

17. (Currently amended) The method of claim 1, wherein the ~~disorder~~ tumor is characterized by ~~unwanted a prostate cell proliferation~~ tumor.

18. (Currently amended) The method of claim 1, wherein the ~~disorder~~ tumor is characterized by ~~a benign unwanted skin proliferation~~ tumor.

/ 19. (Canceled)

20. (Original) The method of claim 1, further comprising increasing TSP-1 activity.

21. (Original) The method of claim 1 or claim 20, further comprising inhibiting VEGF activity.

22. (Original) The method of claim 1, further comprising administering a chemotherapeutic agent.

23. (Original) The method of claim 22, wherein the chemotherapeutic agent is taxol or carboplatin.

/ 24.-52. (Canceled)

53. (Previously presented) The method of claim 1, wherein the fragment is up to 100 amino acids in length.

Applicant : Michael J. Detmar et al.
Serial No. : 09/536,087
Filed : March 24, 2000
Page : 5 of 22

Attorney's Docket No.: 10287-051001 / MGH 1470.0

54. (Previously presented) The method of claim 53, wherein the fragment is up to 50 amino acids in length.

55. (Previously presented) The method of claim 1, wherein the fragment is at least 50 amino acids in length.

56. (Previously presented) The method of claim 1, wherein the fragment is at least 100 amino acids in length.

57. (Previously presented) The method of claim 1, wherein the fragment is at least 200 amino acids in length.

58. (Previously presented) The method of claim 1, wherein the fragment comprises at least one type I repeat.

59. (Previously presented) The method of claim 1, wherein the fragment includes between about 5 to 50 amino acids of a type I repeat.

60. (Previously presented) The method of claim 1, wherein the fragment comprises at least one sequence selected from the group of: amino acids 382-429 of SEQ ID NO:2, amino acids 438-490 of SEQ ID NO:2, and amino acids 495-547 of SEQ ID NO:2.

61. (Previously presented) The method of claim 1, wherein the fragment comprises SEQ ID NO:11.

62. (Canceled)

Applicant : Michael J. Detmar et al.
Serial No. : 09/536,087
Filed : March 24, 2000
Page : 6 of 22

Attorney's Docket No.: 10287-051001 / MGH 1470.0

63. (Previously presented) The method of claim 1, wherein the fragment comprises a procollagen domain or a fragment thereof having the ability to inhibit endothelial cell migration.

64. (Previously presented) The method of claim 1, wherein the fragment comprises
SEQ ID NO:6.

65. (Previously presented) The method of claim 1, wherein the fragment comprises
SEQ ID NO:7.

66. (Previously presented) The method of claim 1, wherein the fragment comprises
SEQ ID NO:8.

67. (Previously presented) The method of claim 1, wherein the fragment comprises
SEQ ID NO:9.

/ 68.-74. (Canceled)

75. (Previously presented) The method of claim 1, wherein the fragment comprises
two type I repeats.

76. (Previously presented) The method of claim 1, wherein the fragment comprises
three type I repeats.

77. (Previously presented) The method of claim 1, wherein the fragment comprises an
amino acid sequence encoded by nucleotides 294-1367 of SEQ ID NO:1. P 28

78. (Previously presented) The method of claim 1, wherein the fragment comprises an
amino acid sequence encoded by nucleotides 294-1883 of SEQ ID NO:1. P 27

Applicant : Michael J. Detmar et al.
Serial No. : 09/536,087
Filed : March 24, 2000
Page : 7 of 22

Attorney's Docket No.: 10287-051001 / MGH 1470.0

79. (Previously presented) The method of claim 1, wherein the fragment comprises an amino acid sequence encoded by nucleotides 1383-1883 of SEQ ID NO:1. 29

80. (Currently amended) The method of claim 1, wherein the ~~disorder~~ tumor is a colon cancer tumor.

81. (Currently amended) The method of claim 1, wherein the ~~disorder~~ tumor is a breast cancer tumor.

82. (Currently amended) The method of claim 1, wherein the ~~disorder~~ tumor is a lung cancer tumor.

83. (Currently amended) The method of claim 1, wherein the ~~disorder~~ tumor is Kaposi's sarcoma.

84. (Previously presented) The method of claim 1, wherein the TSP-2 has an amino acid sequence at least 95% identical to the sequence of SEQ ID NO:2.

85. (Previously presented) The method of claim 1, wherein the TSP-2 has an amino acid sequence at least 98% identical to the sequence of SEQ ID NO:2.

86. (Previously presented) The method of claim 1, wherein the TSP-2 has an amino acid sequence at least 99% identical to the sequence of SEQ ID NO:2.

87. (Currently amended) A method of treating a subject having a ~~disorder~~ characterized by unwanted cell proliferation an angiogenesis-dependent tumor, the method comprising:

Applicant : Michael J. Detmar et al.
Serial No. : 09/536,087
Filed : March 24, 2000
Page : 8 of 22

Attorney's Docket No.: 10287-051001 / MGH 1470.0

identifying a subject having ~~a disorder characterized by unwanted cell proliferation~~ an angiogenesis-dependent tumor; and

administering to the subject a polypeptide comprising the amino acid sequence of SEQ ID NO:2 (TSP-2) or a fragment thereof capable of inhibiting endothelial cell migration, wherein the fragment comprises at least 10 contiguous amino acids of either (a) a procollagen domain of TSP-2, or (b) a type I repeat of TSP-2.

* 88. (New) The method of claim 87, wherein the fragment comprises the sequence of SEQ ID NO:10 (WSPWAEW).

89. (New) The method of claim 87, wherein the tumor is an epithelial tissue tumor.

90. (New) The method of claim 87, wherein the tumor is a skin tumor.

91. (New) The method of claim 90, wherein the tumor is a squamous cell carcinoma of the skin or a malignant melanoma.

92. (New) The method of claim 87, wherein the tumor is a prostate tumor.

93. (New) The method of claim 87, wherein the tumor is a benign skin tumor.

94. (New) The method of claim 87, further comprising increasing TSP-1 activity.

95. (New) The method of claim 87 or claim 94, further comprising inhibiting VEGF activity.

96. (New) The method of claim 87, further comprising administering a chemotherapeutic agent.

Applicant : Michael J. Detmar et al.
Serial No. : 09/536,087
Filed : March 24, 2000
Page : 9 of 22

Attorney's Docket No.: 10287-051001 / MGH 1470.0

97. (New) The method of claim 96, wherein the chemotherapeutic agent is taxol or carboplatin.
98. (New) The method of claim 87, wherein the fragment is up to 100 amino acids in length.
99. (New) The method of claim 98, wherein the fragment is up to 50 amino acids in length.
100. (New) The method of claim 87, wherein the fragment is at least 50 amino acids in length.
101. (New) The method of claim 87, wherein the fragment is at least 100 amino acids in length.
102. (New) The method of claim 87, wherein the fragment is at least 200 amino acids in length.
103. (New) The method of claim 87, wherein the fragment comprises at least one type I repeat.
104. (New) The method of claim 87, wherein the fragment includes between about 5 to 50 amino acids of a type I repeat.
105. (New) The method of claim 87, wherein the fragment comprises at least one sequence selected from the group of: amino acids 382-429 of SEQ ID NO:2, amino acids 438-490 of SEQ ID NO:2, and amino acids 495-547 of SEQ ID NO:2.

Applicant : Michael J. Detmar et al.
Serial No. : 09/536,087
Filed : March 24, 2000
Page : 10 of 22

Attorney's Docket No.: 10287-051001 / MGH 1470.0

106. (New) The method of claim 87, wherein the fragment comprises SEQ ID NO:11.
107. (New) The method of claim 87, wherein the fragment comprises a procollagen domain or a fragment thereof having the ability to inhibit endothelial cell migration.
108. (New) The method of claim 87, wherein the fragment comprises SEQ ID NO:6.
109. (New) The method of claim 87, wherein the fragment comprises SEQ ID NO:7.
110. (New) The method of claim 87, wherein the fragment comprises SEQ ID NO:8.
111. (New) The method of claim 87, wherein the fragment comprises SEQ ID NO:9.
112. (New) The method of claim 87, wherein the fragment comprises a fragment of SEQ ID NO:10 at least 4 amino acids in length.
113. (New) The method of claim 87, wherein the fragment comprises two type I repeats.
114. (New) The method of claim 87, wherein the fragment comprises three type I repeats.
115. (New) The method of claim 87, wherein the fragment comprises an amino acid sequence encoded by nucleotides 294-1367 of SEQ ID NO:1.
116. (New) The method of claim 87, wherein the fragment comprises an amino acid sequence encoded by nucleotides 294-1883 of SEQ ID NO:1.

Applicant : Michael J. Detmar et al.
Serial No. : 09/536,087
Filed : March 24, 2000
Page : 11 of 22

Attorney's Docket No.: 10287-051001 / MGH 1470.0

117. (New) The method of claim 87, wherein the fragment comprises an amino acid sequence encoded by nucleotides 1383-1883 of SEQ ID NO:1.

118. (New) The method of claim 87, wherein the tumor is a colon tumor.

119. (New) The method of claim 87, wherein the tumor is a breast tumor.

120. (New) The method of claim 87, wherein the tumor is a lung tumor.

121. (New) The method of claim 87, wherein the tumor is Kaposi's sarcoma.

122. (New) A method of treating an angiogenesis-dependent tumor, the method comprising administering to the subject a fragment of TSP-2 consisting of the sequence of SEQ ID NO: 10 (WSPWAEW).
